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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 2632-1-001

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on October 28, 2008

Signature Michele Hofherr

Typed or printed name Michele Hofherr

Application Number	Filed
09/980,649	June 4, 2002

First Named Inventor: Pierre Belhumeur

Art Unit	Examiner
1651	Kim, Taeyoon

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 39,839
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

J. David Smith
Signature

J. David Smith
Typed or printed name

201-487-5800
Telephone number

October 28, 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 3 forms are submitted.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Pierre Belhumeur, *et al.*	Art Unit:	1651
Serial Number:	09/980,649	Examiner:	Kim, Taeyoon
Filing Date:	June 4, 2002		
For:	BIOLOGICAL INDICATORS FOR VALIDATING A PRION STERILIZATION PROCESS		

CERTIFICATE OF MAILING UNDER 37 CFR 1.8

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Michele Hofherr (Name of Person Depositing Mail)

Michele Hofherr 10-28-08 (Signature and Date)

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop BOX AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Please find enclosed herewith form PTO/SB/33, a Pre-Appeal Brief Request for Review. Please consider the reasons below for which the review is being requested. A Notice of Appeal is being filed concurrently.

REASONS:

1. The Examiner has failed to set forth a proper *prima facie* case of obviousness for any of the rejected claims 3 and 5-15.

2. Claims 3 and 5-15 are patentable under 35 USC 103(a) over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.*

3. Claim 9 is patentable under 35 USC 103(a) over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.* in further view of Feldman *et al.*

4. Claims 9, 10 and 13 are patentable under 35 USC 103(a) over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.* and further in view of Dresdner *et al.*

The Examiner declined a telephone interview with the inventors prior to the filing of this Pre-Appeal Brief Request for Review. In the Advisory Action issued on September 26, 2008, the Examiner acknowledges that in the Response to the Final Office Action, filed August 28, 2008, Applicants explained that the presently claimed invention is a method for evaluating the efficiency of a sterilization process whereas Safar *et al.* teach methods to study the thermal stability and conformational transitions of scrapie amyloid protein and their correlation with infectivity. The Examiner acknowledges that the current claims are drawn to a method of subjecting a prion protein to a degradation indicator and determining the level of degradation thereof. The Examiner alleges that Safar *et al.* teach the same method step since Safar *et al.* teach a method of subjecting a scrapie amyloid protein, which is a prion, to thermal exposure and evaluating the inactivity of the treated prion protein. Thus, the Examiner alleges that the process of Safar *et al.* is substantially similar, if not identical, to the presently claimed method. The Examiner also disagrees with Applicants' explanations that the yeast prion proteins of the current invention are not analogs of their mammalian counterpart, and that there is no teaching, motivation or suggestion to substitute the prion protein of Safar *et al.* with a yeast prion. The Examiner considers that since yeast proteins are recognized as "prion proteins" and known as analogs of the mammalian counterpart in the art, it would have been obvious to one of ordinary skill in the art to try the yeast prion proteins in the place of mammalian prion proteins.

1. <u>The references when combined do not teach or suggest the presently claimed methods.</u>

A. Regarding measuring degradation

Applicants submit that the references, when combined, do not produce the presently claimed methods. As such, the Examiner has failed to set forth a proper *prima facie* case of obviousness. Applicants respectfully reiterate that the goal of ***Safar et al.*** was to ***study the thermal stability and conformational transitions of scrapie amyloid protein and its correlation with infectivity***. To this end, Safar *et al.* submitted a scrapie amyloid protein to heat treatment and to chemical scrapie inactivators such as FA, SDS, additional α-helix-inducing fluorinated alcohols and TFA to measure their effect on the conformation of PrP27-30 and the ability to propagate,

replicate and cause disease. One of ordinary skill in the art would agree that analyzing the results of Safar *et al.*, particularly Figure 1 where the effect of heat and formic acid on PrP27-30 is visualized by silver staining and Western blot, reveals that Safar *et al.* only demonstrate a conformational transition of scrapie amyloid protein which they correlate with a reduction in infectivity. ***Safar et al. do not teach or suggest the degradation of a prion protein***. On the contrary, the protein level visualized by silver staining and Western blot reported by Safar *et al.* is clearly not changed. (See, Fig. 1) Therefore, ***Safar et al. do not measure degradation***. Rather, ***Safar et al. measure a conformational change*** which they correlate with the infectivity level of the prion. Safar *et al.* do not make a correlation between the infectivity level of the prion and its degradation.

The presently claimed method is for evaluating the efficiency of a sterilization process. Since some sterilization processes allow a significant degradation of prion proteins whereas other methods produce a weaker degradation, the method claimed in the present application allows the evaluation of the efficacy of different sterilization processes. ***The presently claimed methods measure***, when using for example ozone, a powerful sterilizing agent, the ***destruction or degradation of a yeast prion.*** Figure 4 of the present specification demonstrates that the prion protein is degraded as no band is observed in the "T" lane on the Western blot. Applicants respectfully submit that for a similar experimental protocol, following the reasoning of the Examiner, a degradation of the prion protein should be observed in Figure 1 of Safar *et al.* That is, degradation of the prion protein should normally be observed as a decrease in the intensity of bands observed in a Western blot. However, contrary to the Examiner's position and contrary to what would be expected if degradation of the prion protein was in fact occurring, degradation is not demonstrated in Figure 1 of Safar *et al.*

B. Regarding replacing mammalian prion proteins with yeast prion proteins

The Examiner maintains that yeast prions are known as mammal prion analogs and thus it would have been obvious to replace the mammalian prion disclosed in Safar *et al.* by a yeast prion. Applicants refer to the Declaration under 37 C.F.R. 1.132 submitted on August 28, 2008 by Dr. Belhumeur, an inventor of the present invention, in order to evidence the contrary. Applicants submit that one or ordinary skill in the art would agree that there are ***significant differences between yeast prion proteins and mammalian prion proteins***. Even though there

may be some belief among some scientists that yeast proteins are analogs of "prion proteins" and known as analogs of mammalian prions, there is still significant uncertainty regarding whether one of ordinary skill in the art could predict the utility of an invention based upon the teachings of Safar *et al.* using the proteins disclosed by Coustou *et al.*, Glover *et al.* or Wickner *et al.*

2. Claims 3 and 5-15 are patentable over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.*

Applicants respectfully submit that the methods of claims 3 and 5-15 are not obvious over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.* for the reasons set forth above. Additionally, the presently claimed methods provide significant advances over the prior art. The presently claimed methods may be adapted to industrial processes having a need to control the efficiency of a sterilization process. By Western Blot analysis, the present specification demonstrates that there is no residual yeast prion protein detectable after ozone treatment. (See, e.g. Table 1 of the instant specification) Ozone treatment goes beyond all the treatments described by Safar *et al.* as ozone is an extremely powerful oxidative process, able to break down chemical bonds. The mere fact of knowing from Safar *et al.* that heat or chemical treatment may have an effect on the conformation of a mammal prion protein is not sufficient to suggest to one of ordinary skill in the art a method of evaluating the efficiency of a sterilization process using proteins described by Coustou *et al.*, Glover *et al.*, or Wickner *et al.* Applicants respectfully suggest that alleging to the contrary constitutes impermissible hindsight.

3. Claim 9 is patentable over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.* in further view of Feldman *et al.*

For the reasons provided above, Applicants submit that the method of claim 9 is not obvious over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.* in further view of Feldman *et al.* The teachings of Safar *et al.* that heat or chemical treatment may affect the ***conformation*** of a mammal prion protein do not teach or suggest a method of evaluating the efficiency of a sterilization process (e.g. using oxidizing agents such as hydrogen as a form of low-temperature gas plasma as in Feldman *et al.*) using proteins described by Coustou *et al.*, Glover *et al.* or Wickner *et al.* As such, the references, when combined, do not produce the presently claimed methods.

4. Claims 9, 10 and 13 are patentable over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.* in further view of Dresdner *et al.*

Similarly, for the reasons provided above, Applicants submit that the methods of claims 9, 10 and 13 are not obvious over Safar *et al.* in view of Coustou *et al.*, Glover *et al.* or Wickner *et al.* in further view of Dresdner *et al.* The teachings of Safar *et al.* that heat or chemical treatment may affect the ***conformation*** of a mammal prion protein do not teach or suggest a method of evaluating the efficiency of a sterilization process (e.g. using ozone or sodium hydroxide as in Feldman et al.) using proteins described by Coustou *et al.*, Glover *et al.* or Wickner *et al.* As such, the references, when combined, do not produce the presently claimed methods.

5. Summary

For the reasons set forth above, Applicants submit that the claims are patentable over Safar *et al.*, Coustou *et al.*, Glover *et al.*, Wickner *et al.*, Feldman *et al.* and Dresdner *et al.* As such, Applicants respectfully submit that the 35 U.S.C. §103(a) rejections over the prior art are improper and request that the rejections be withdrawn. Applicants submit, therefore, that the claims are in condition for allowance, and prompt action in the form of a Notice of Allowance is earnestly solicited.

Respectfully submitted,

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